



# *THE BAMBINO GESU' CHILDREN'S HOSPITAL and e-HEALTH.*

*The diagnostic and predictive contribution of Health-e-Child within the heuristic perspective of the Virtual Physiological Human framework*



## Genetic Results

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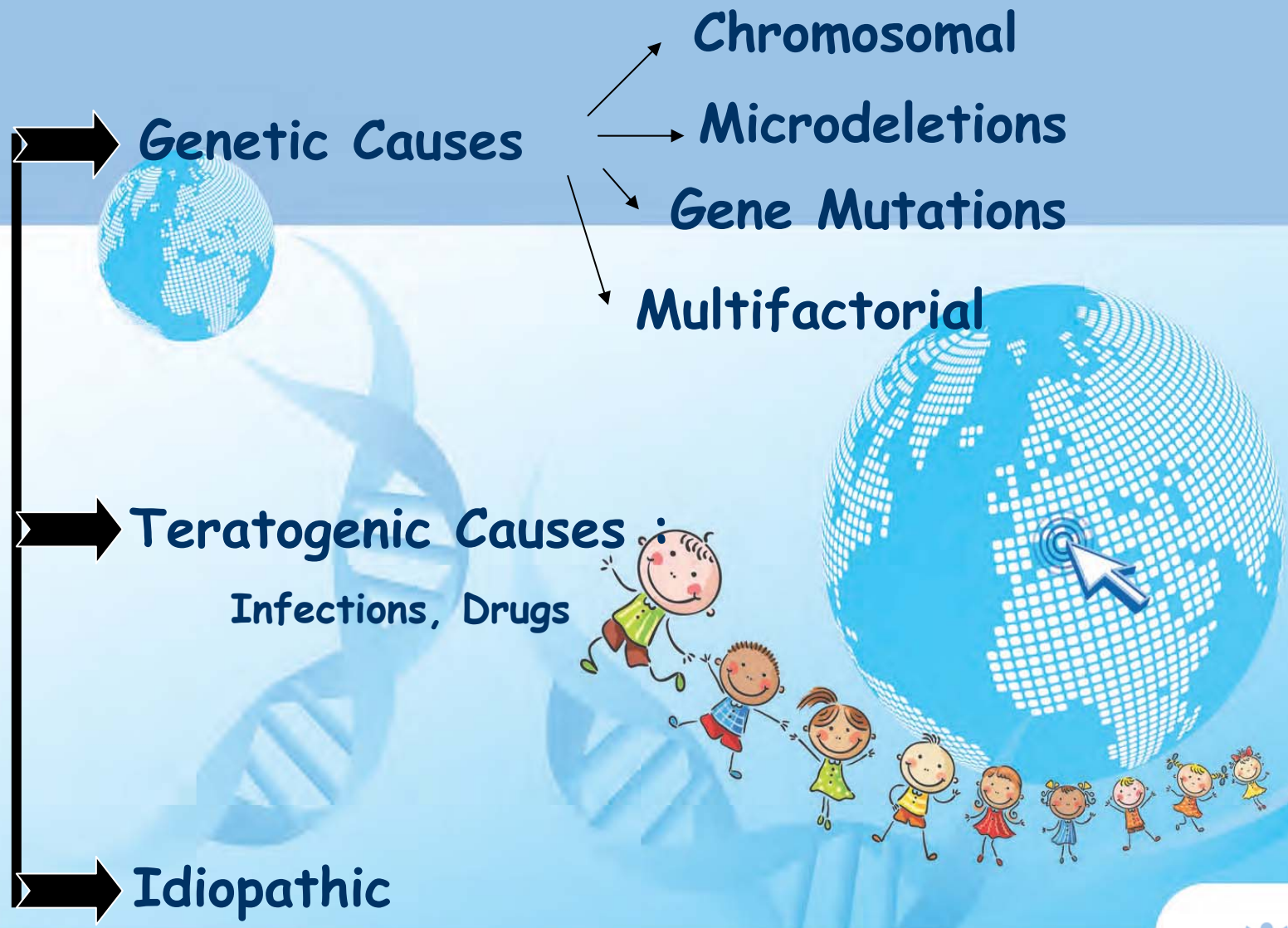


## **Congenital Heart Diseases (CHD): Relevance to Children's Health**

- Prevalence 5-10/1000 livebirths**
- 10% of pediatric mortality**
- 50% of death secondary to malformation**



# CHD



# The Bambino Gesù Research Team

- Principal objective:
  - Contribute to the genetic diversity of CHD
- Secondary objectives:
  - Identify variants in candidate genes in ToF
  - Perspective of the other genome (mtDNA)



# The Bambino Gesù Research Team

## RIGHT VENTRICULAR OVERLOAD CHD (RVO)



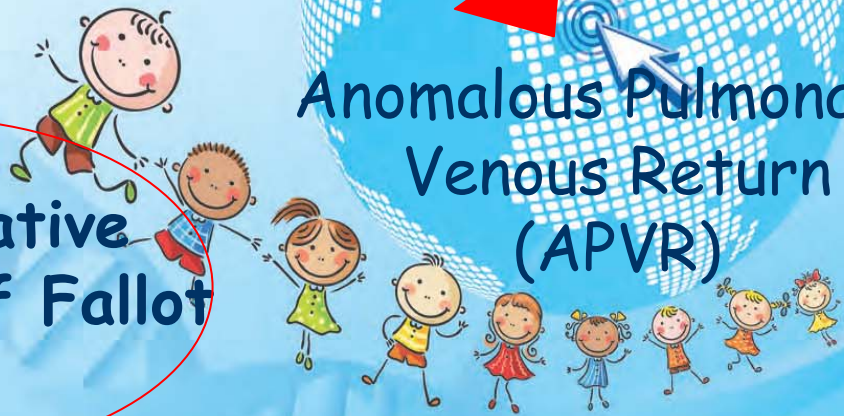
Atrial Septal Defects (ASD)



Post-operative Tetralogy of Fallot (ToF)



Anomalous Pulmonary Venous Return (APVR)

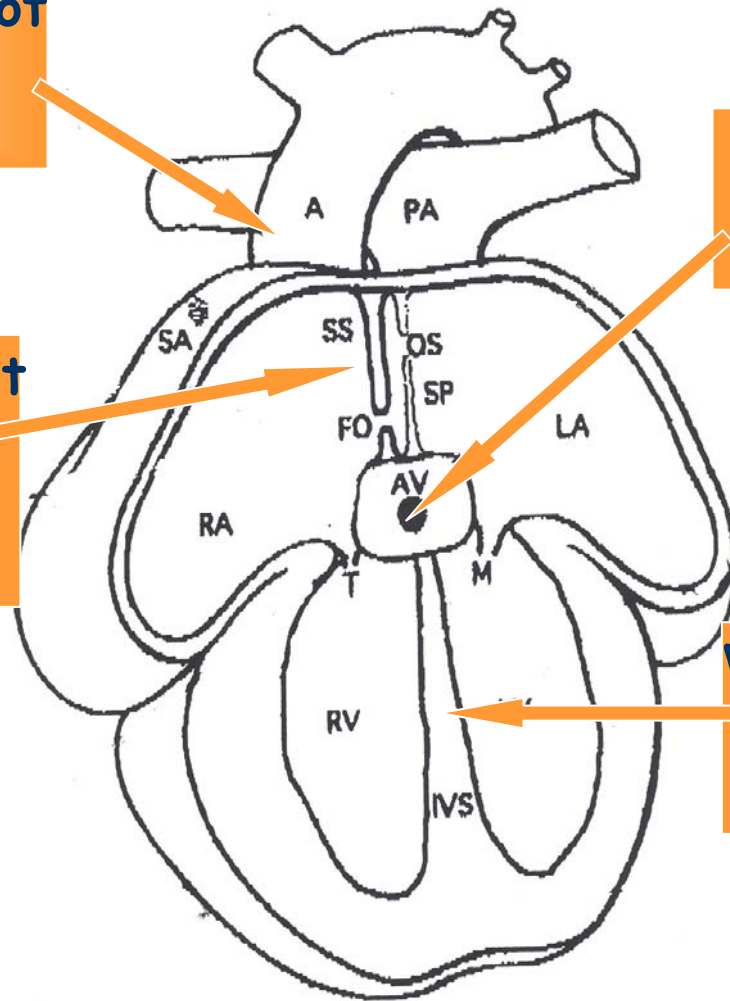


## A candidate gene approach

**Tetralogy of Fallot**  
*NKX2.5*  
*GATA4*

**Atrioventricular Block**  
*NKX2.5*  
*TBX5*

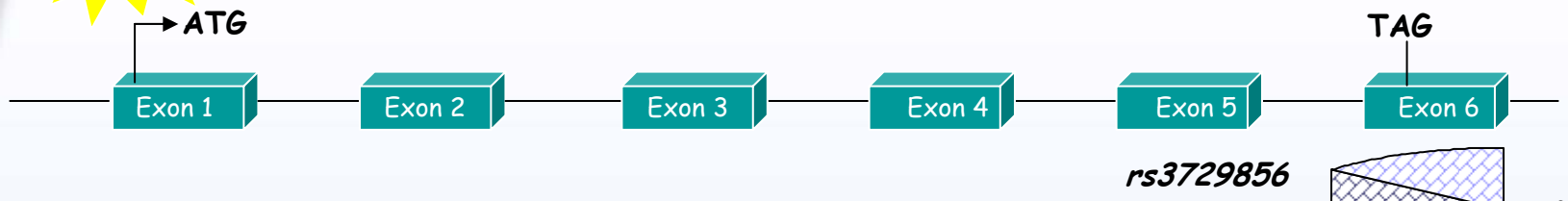
**Atrial Septal Defect**  
*GATA4*  
*NKX2.5*  
*TBX5*



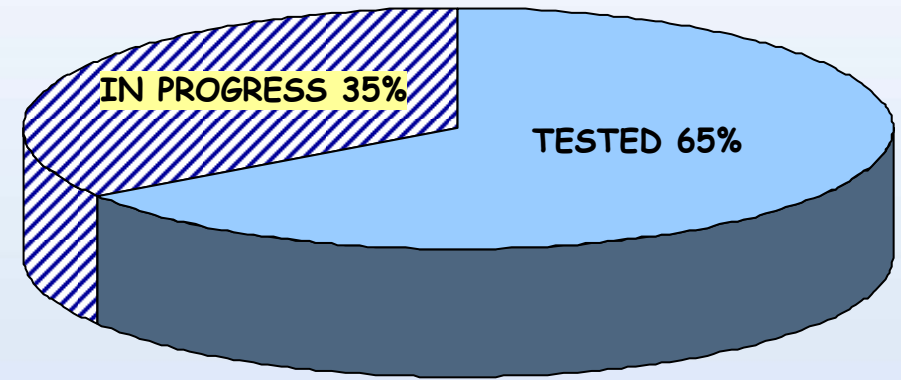
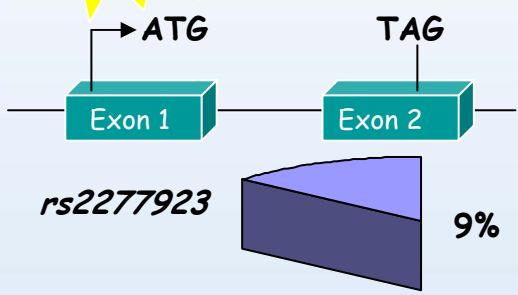
**Ventricular Septal Defect**  
*TBX5*  
*NKX2.5*

# Genetic Results: July 08-July 09

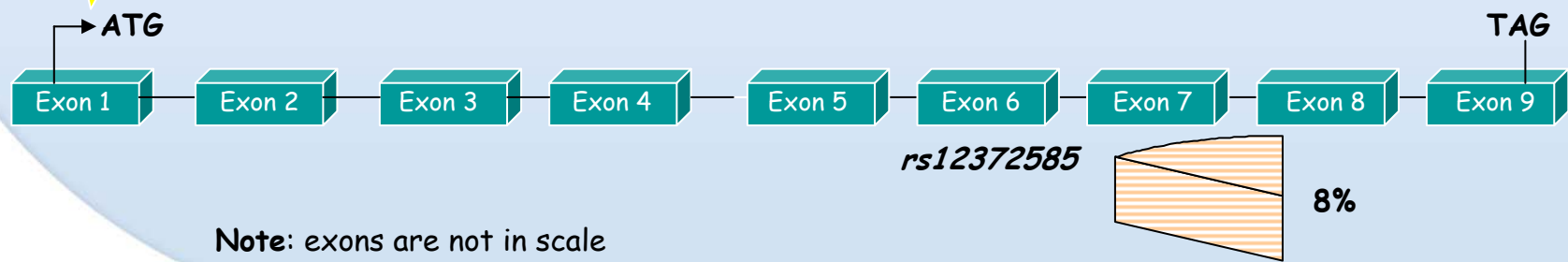
**GATA4**



**NKX2.5**

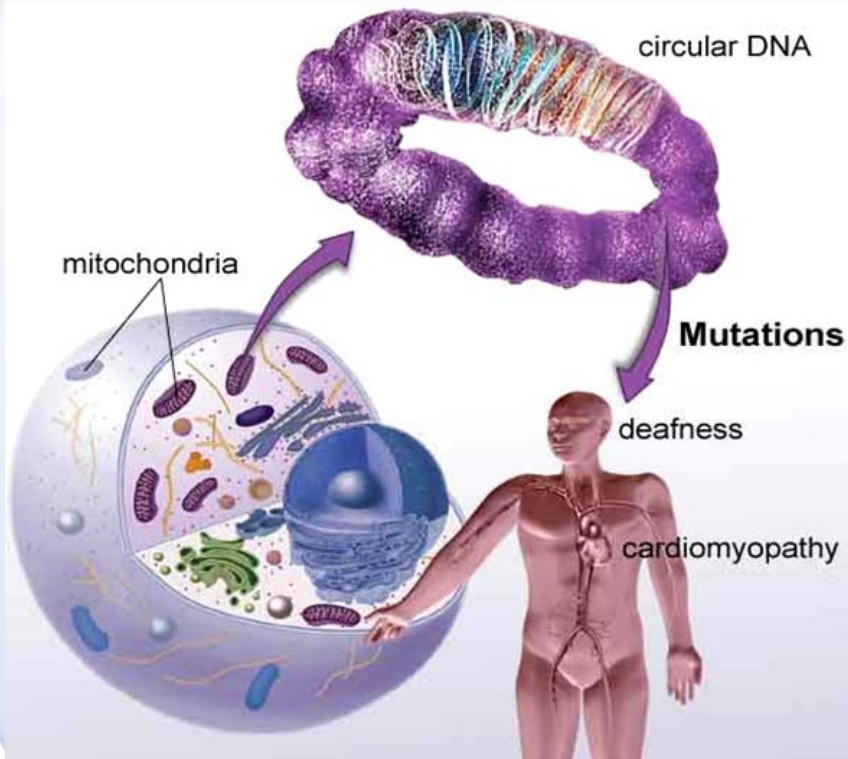


**TBX5**



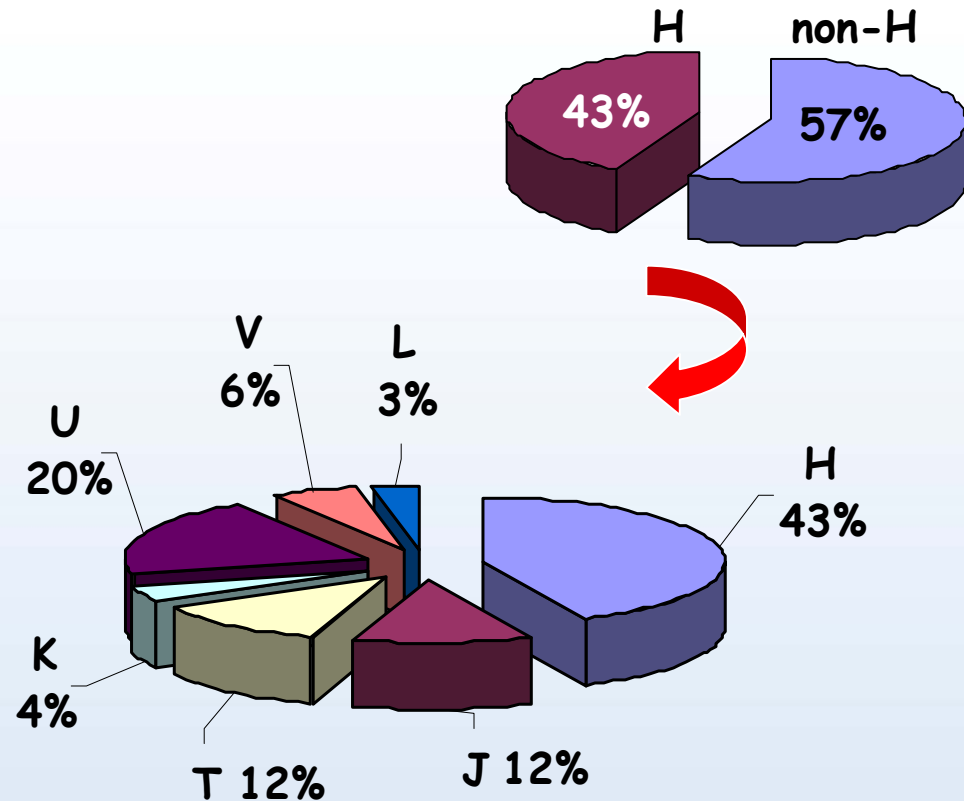
Note: exons are not in scale

## The hidden side of the cell



- The mitochondrial genome is another good candidate because of the central role played by mitochondrial genes in OXPHOS and cell metabolism.
- Heart conditions leading to hypoxia and contractile failure have impaired metabolism with  $\downarrow$  [ATP] and  $\uparrow$  [Lactate].
- Impaired OXPHOS activities are found in ToF.

- A characteristic of the mitochondrial genome (mtDNA) is the high level of interindividual variability that ensues from high mutation rate and unilinear inheritance.
- Combination of polymorphic variants of mtDNA can affect rate, severity and quality of human diseases.



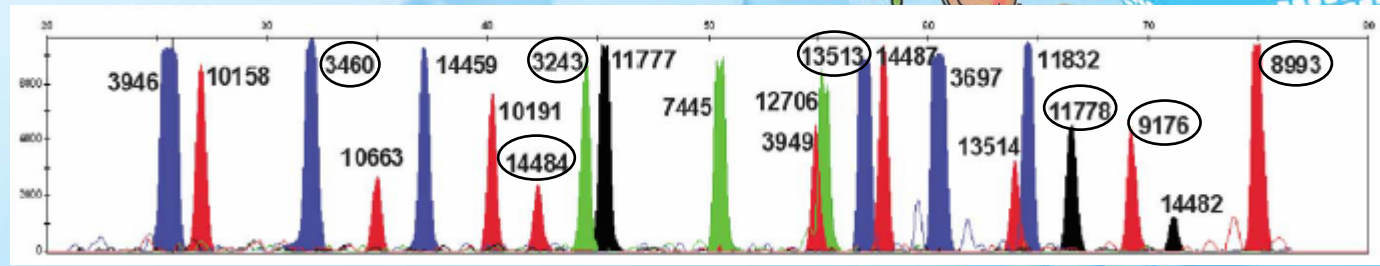
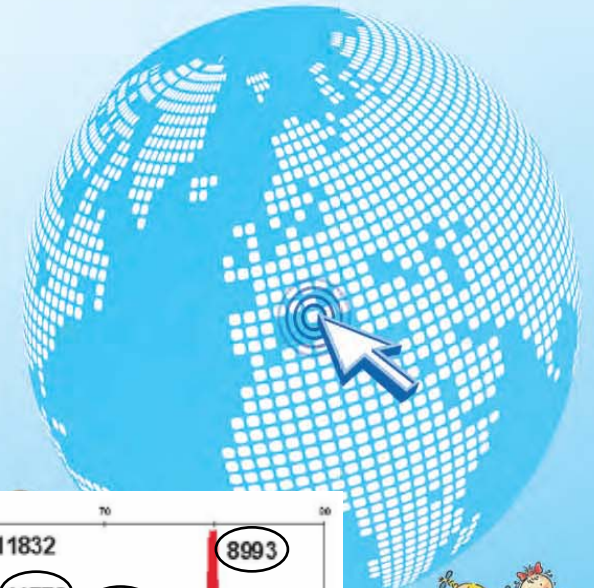
Note: Frequencies in 44/81(54%) cases



# Multiple minisequencing



- Single tube reaction
- Use tiny amount of DNA



Thank you for your attention

With the key contribution of:

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